

Scheme A



FIG. 1

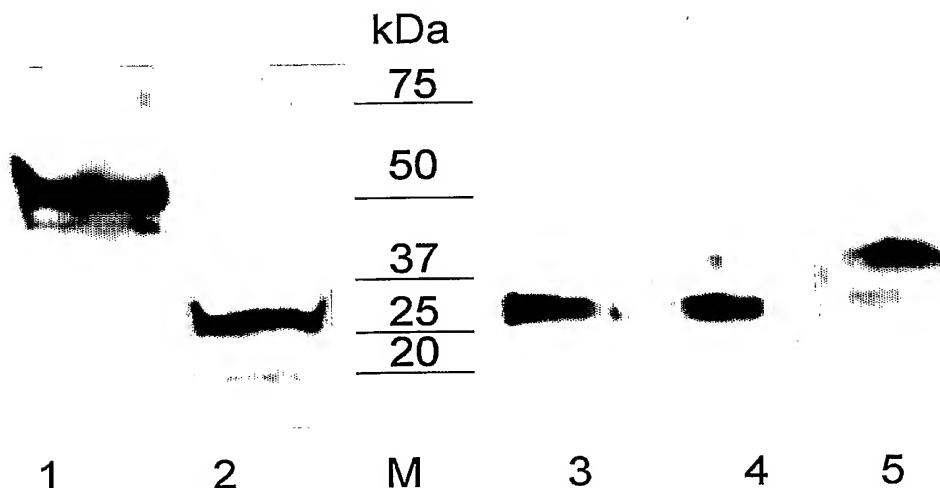


FIG. 2

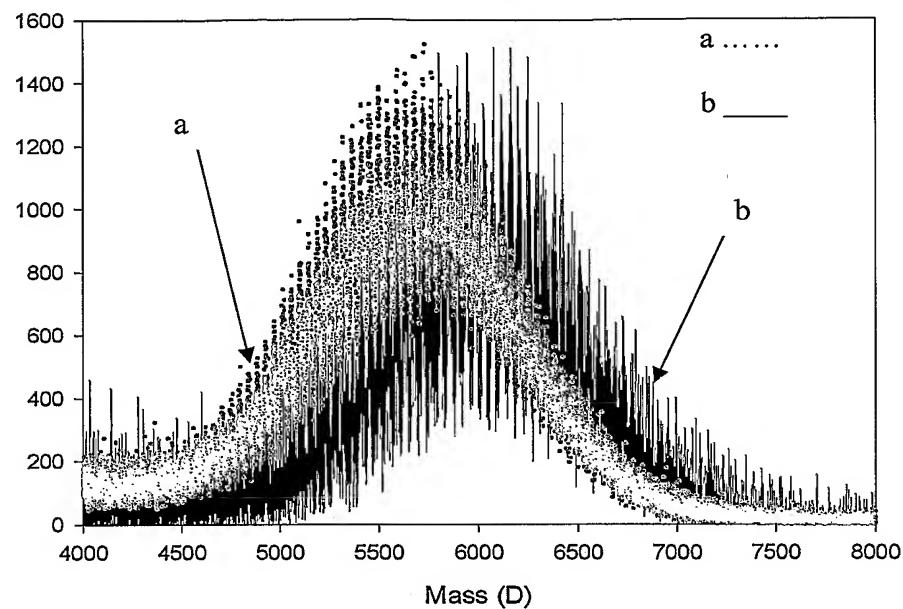


FIG. 3 (in color)

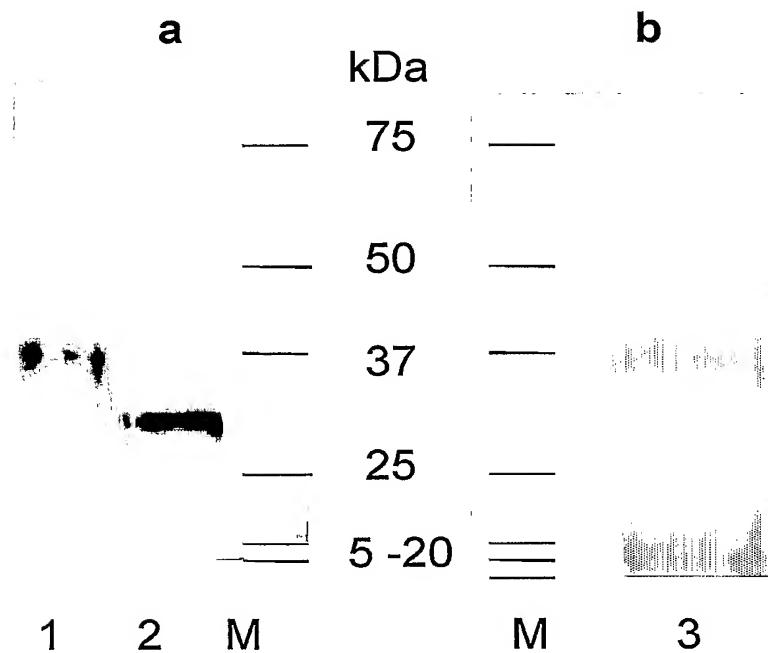
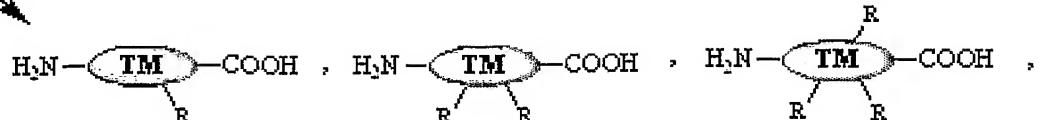


FIG. 4

Genetically Directed Synthesis
using non-natural amino-acid :



TM analogs containing NNAA

TM: Thrombomodulin analog capable of activating protein C

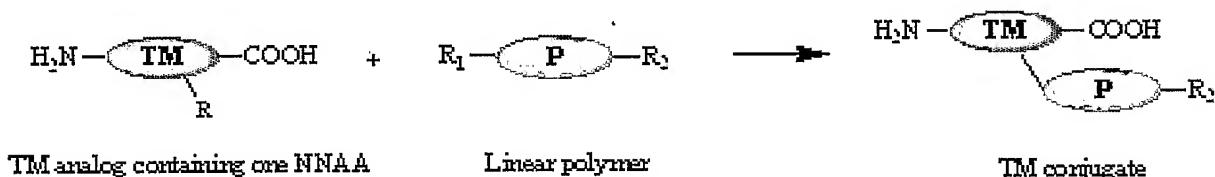
NH₂: Amino group at the N-terminal of TM

COOH: Carboxylic acid group C-terminal of TM

NNAA: Non-Natural Amino Acid

R: Functional group of the non-natural amino acid (N₃, alkyl, diene, ...)

Example of a Conjugation Reaction:

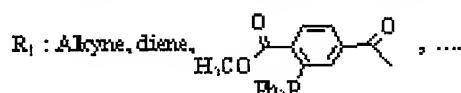


TM analog containing one NNAA

Linear polymer

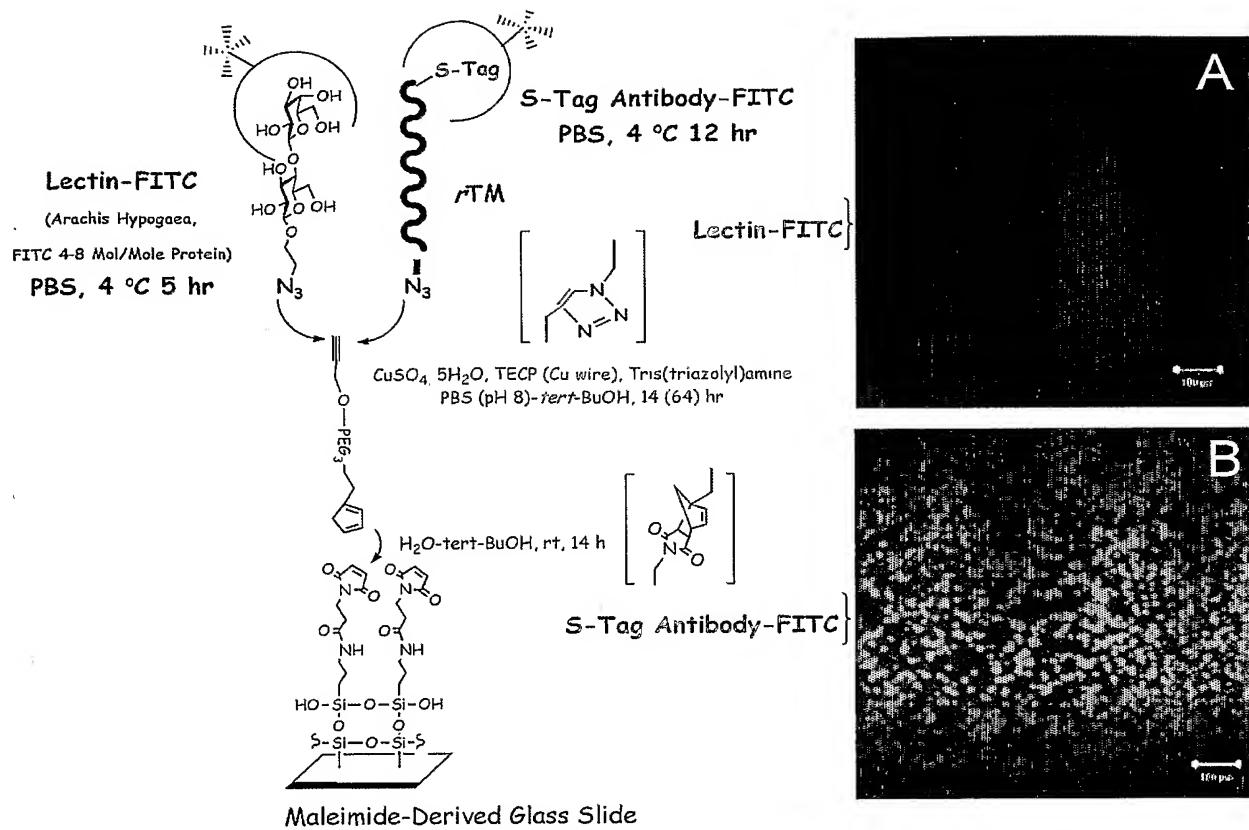
TM conjugate

P: Linear or branched natural or synthetic polymers such as PEG, oligosaccharides, ...

 R_2 : Functional group for anchoring onto surface : alkyne, diene, biotin, ...

- Anti-inflammatory/anti-thrombotic groups such as heparin, sialic acid Lewis X, ...

FIG. 5

**FIG. 6 (in color)**